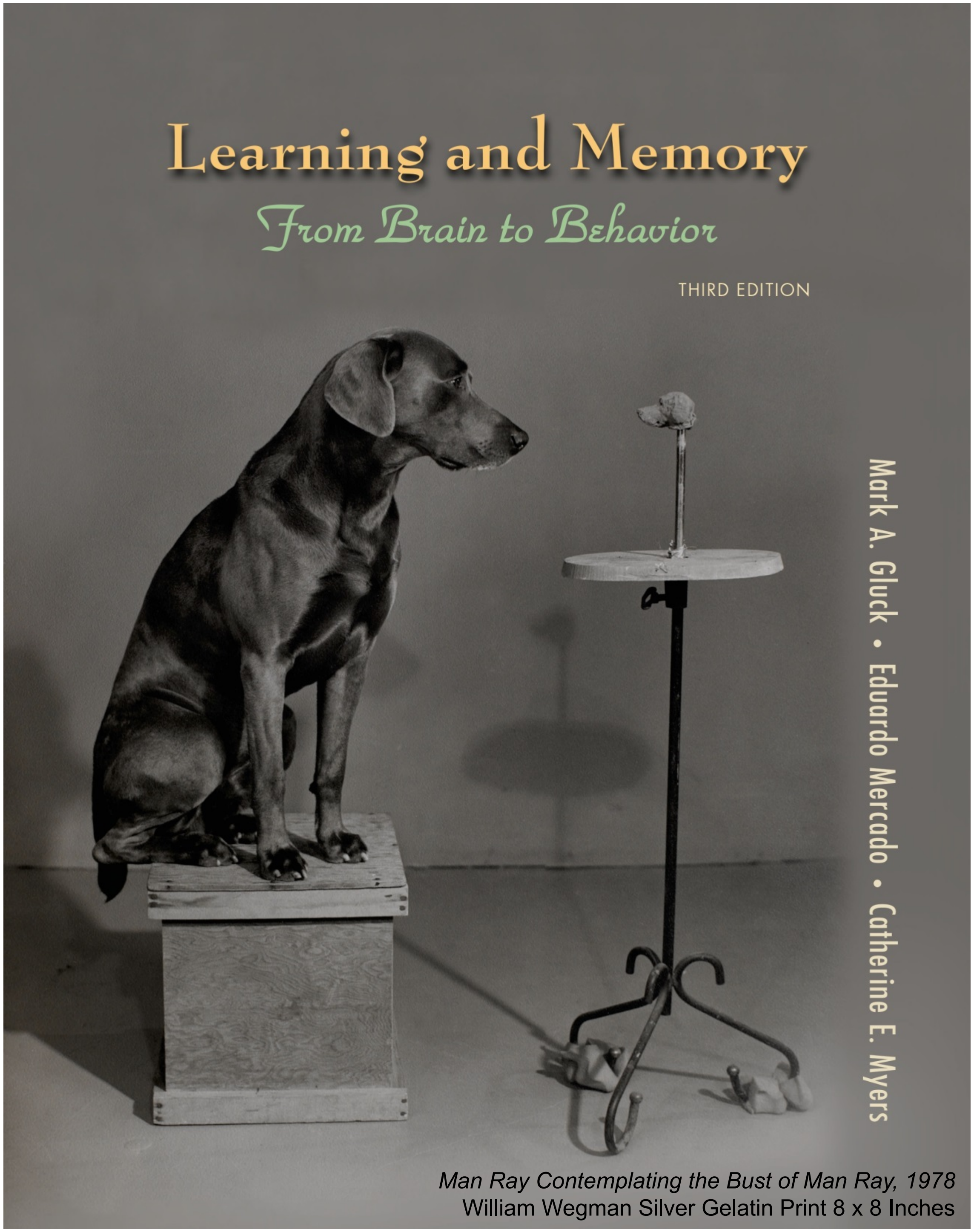

Chapter 2

The Neuroscience of Learning and Memory

Slides prepared by
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University of Central Florida

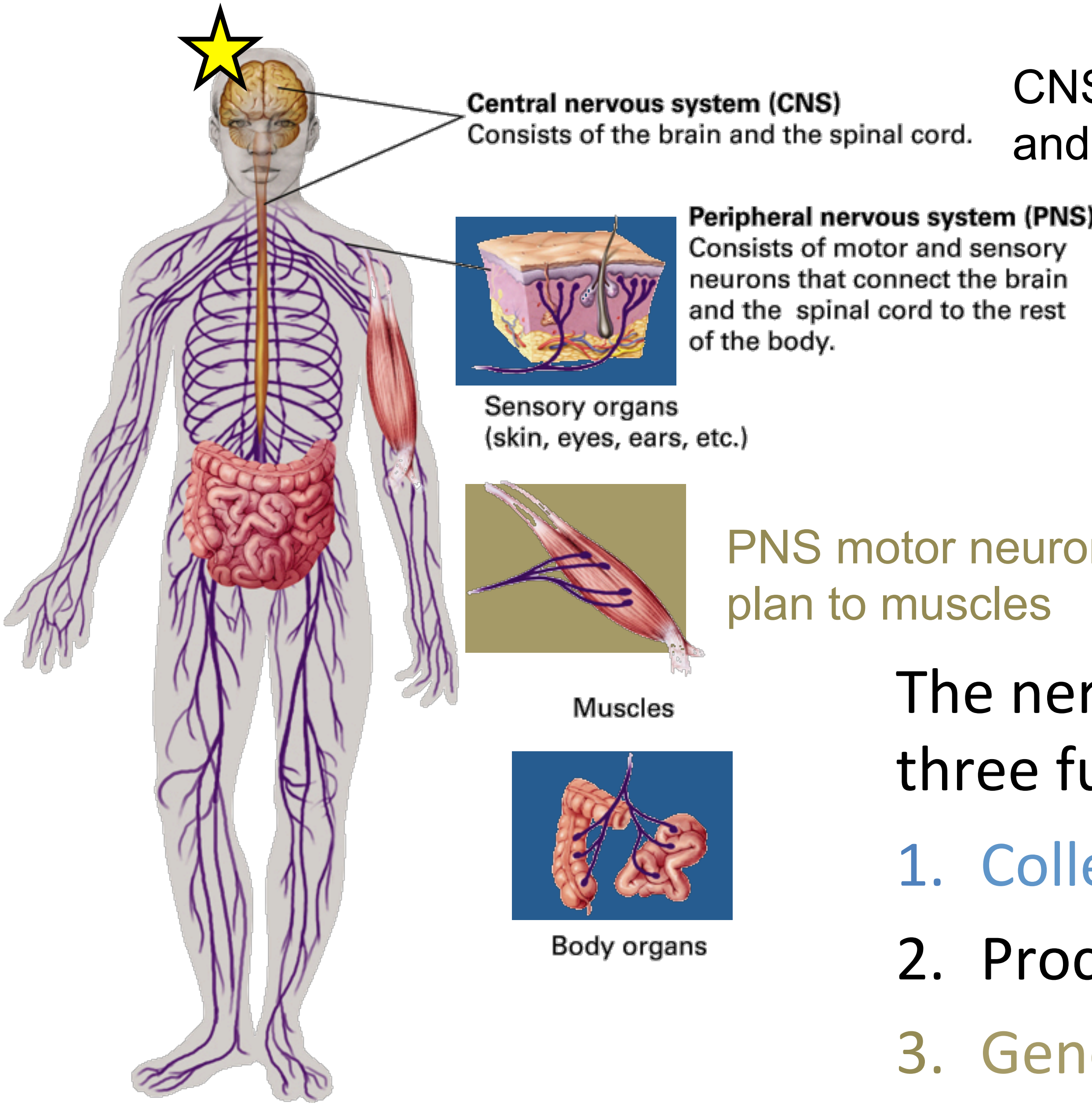
The Neuroscience of Learning and Memory

- Structural properties of the nervous system
- Functional properties of learning and memory systems
- Manipulating nervous system activity

What are the major divisions of the brain and their functions?

* **neuroscience:** the scientific study of the brain and the rest of the nervous system

Structural Properties of Nervous Systems



CNS processes information and generates behavioral plan

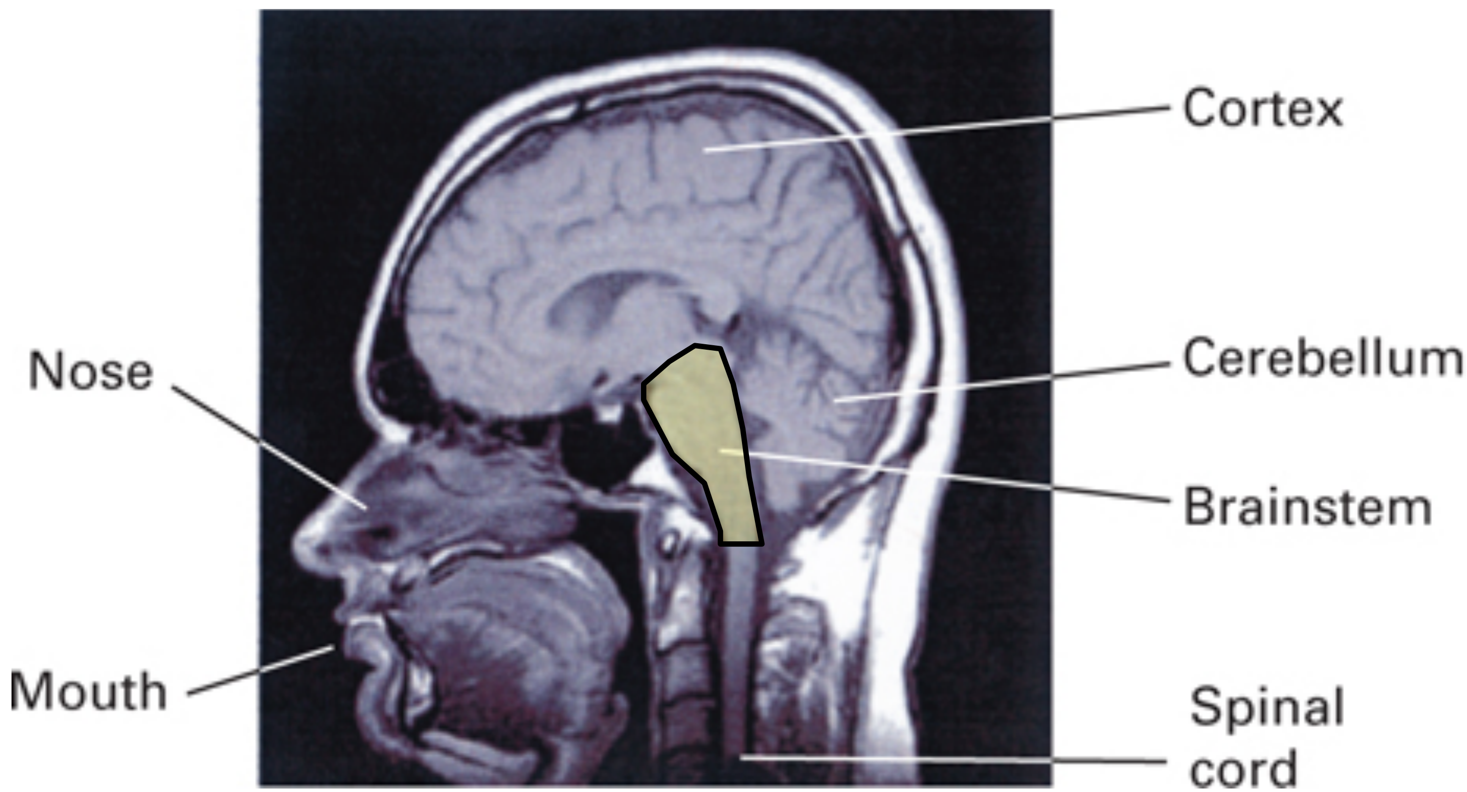
PNS sensory neurons collect information

PNS motor neurons relay behavioral plan to muscles

The nervous system has three functions:

1. Collect information
2. Process information
3. Generate behavior

The Human Brain



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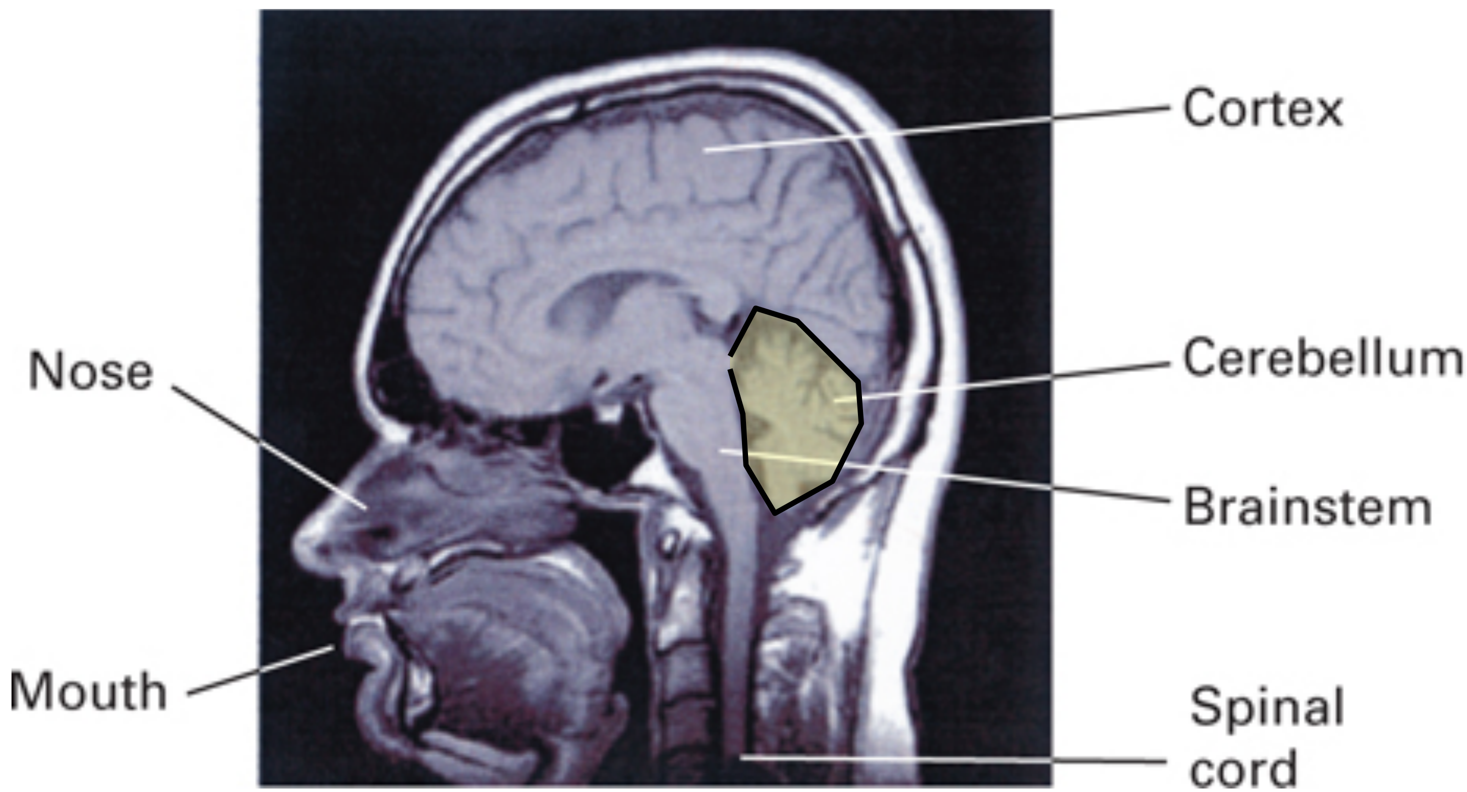
The **brainstem** sits atop the spinal cord. It connects the brain and spinal cord and completes many basic physiological functions, such as breathing and digestion.

The Human Brain Part 2



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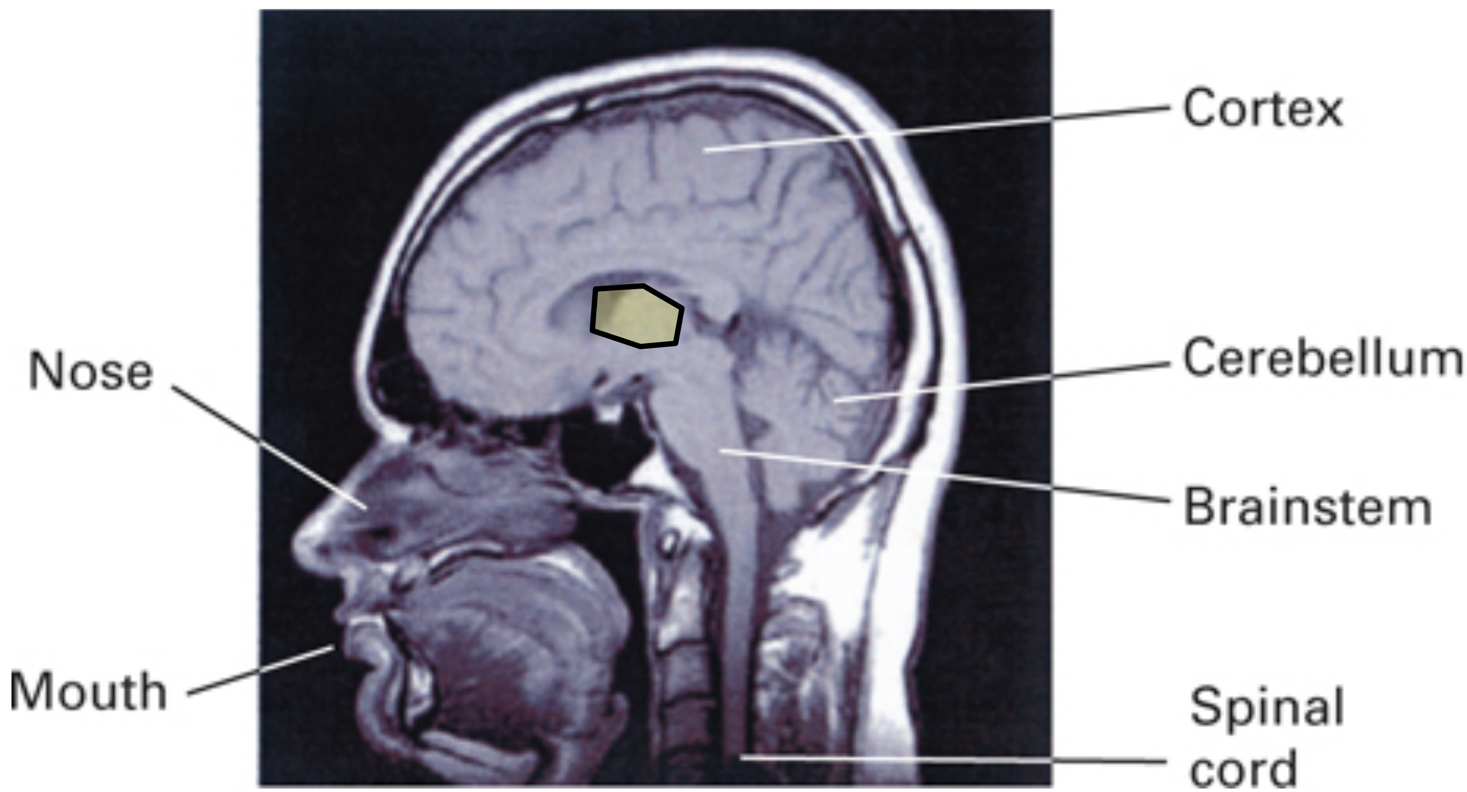
The **cerebellum** (*little brain*) is important for motor control and coordination.

The Human Brain Part 3



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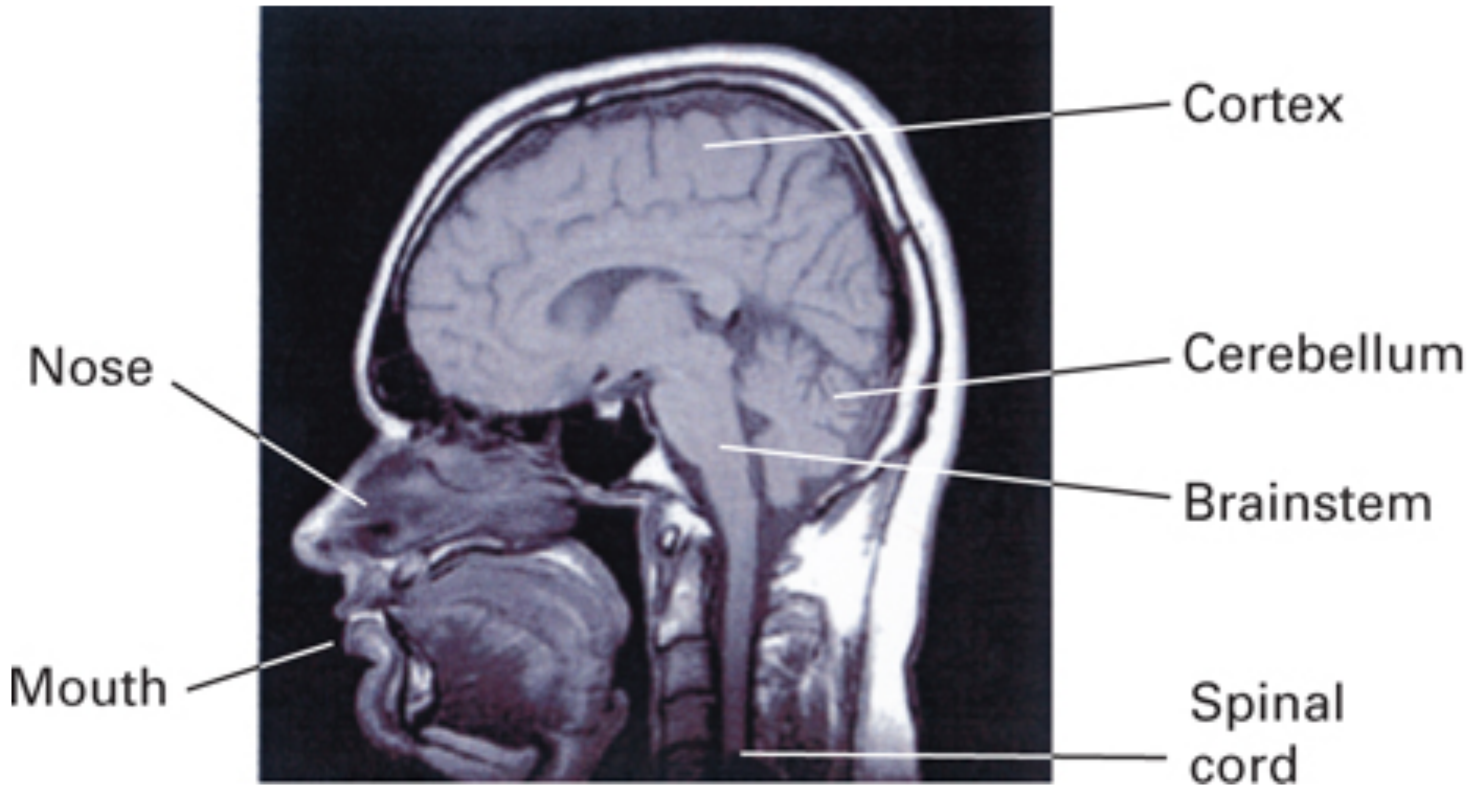
Subcortical structures are between the brain stem and cortex.

- The **thalamus** (*the egg*) relays sensory information to the brain.

The Human Brain Part 4



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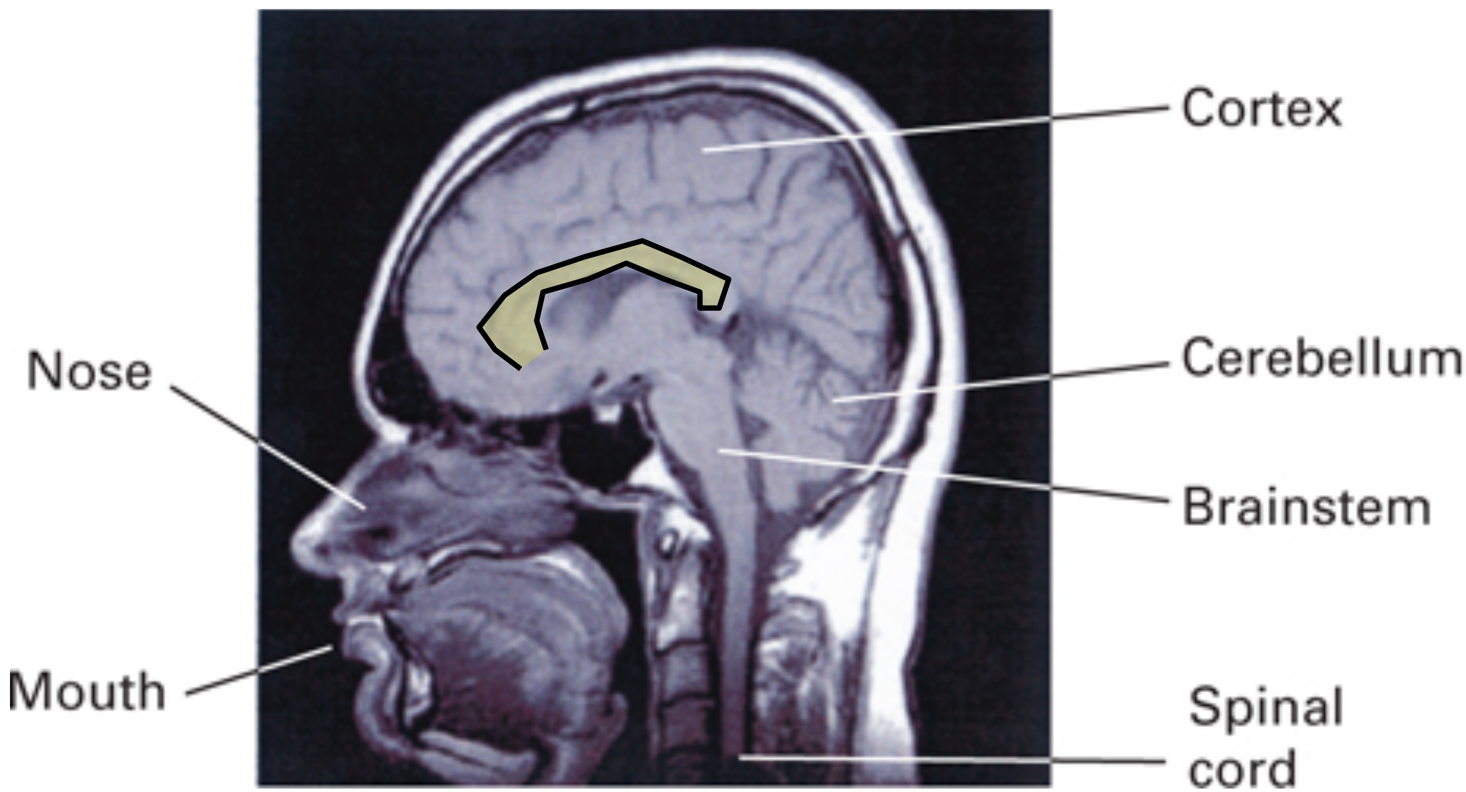
Subcortical structures not shown on this slide:

- **Basal ganglia** – planning and producing skilled movements
- **Hippocampus** *(the seahorse*) – learning new facts
- **Amygdala** *(the almond*) – emotional memories

The Human Brain Part 5



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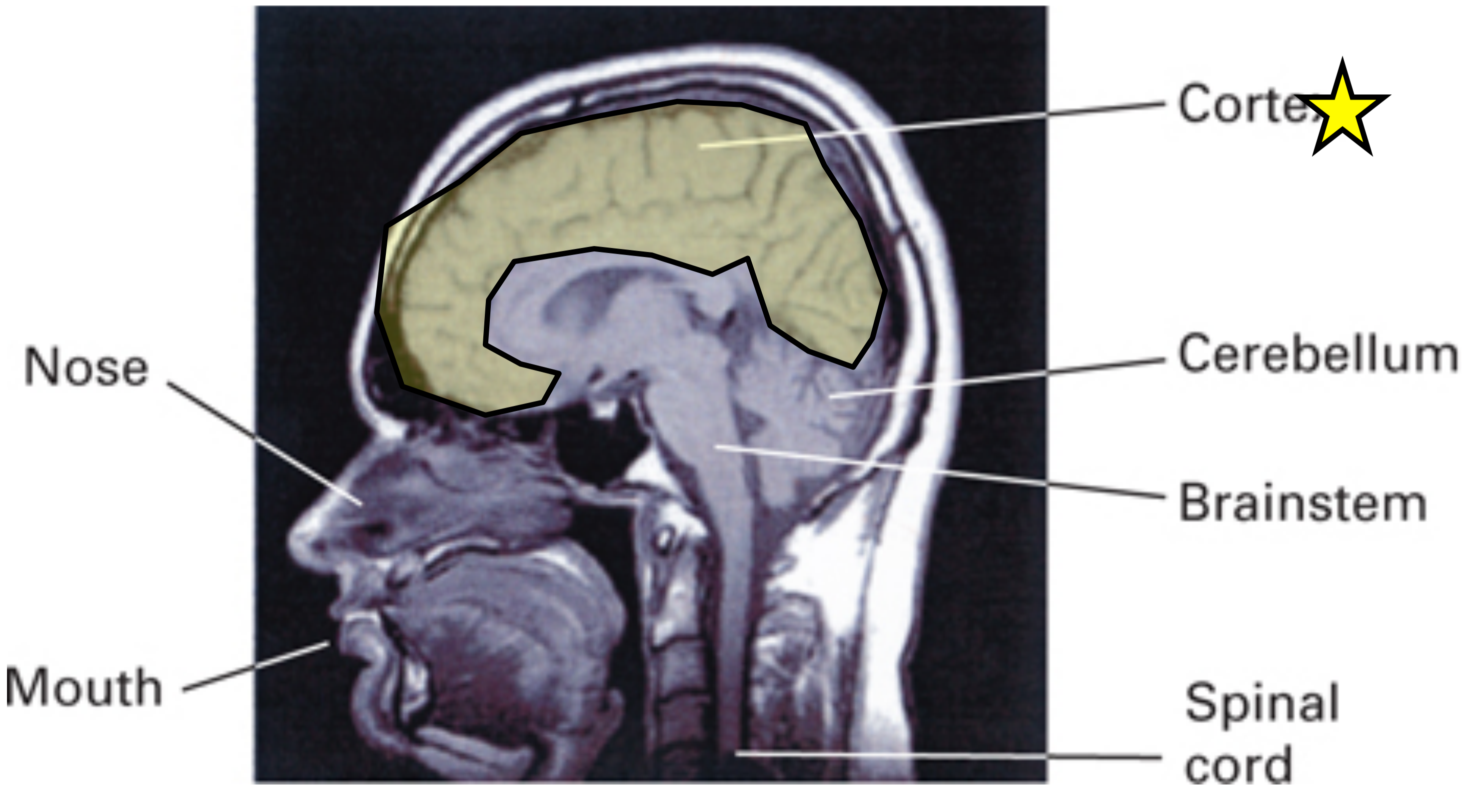
Subcortical white matter – massive tracts of neural wiring connecting regions of cortex to other brain areas (especially other parts of cortex)

- **Corpus callosum** – connects cortex of the two **hemispheres**

The Human Brain Part 6



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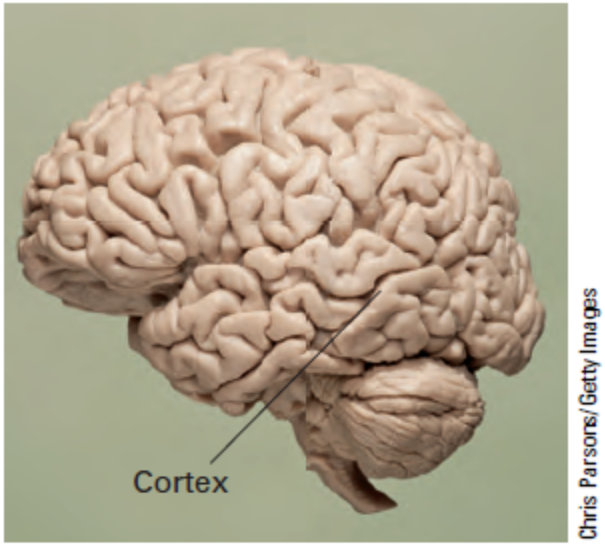
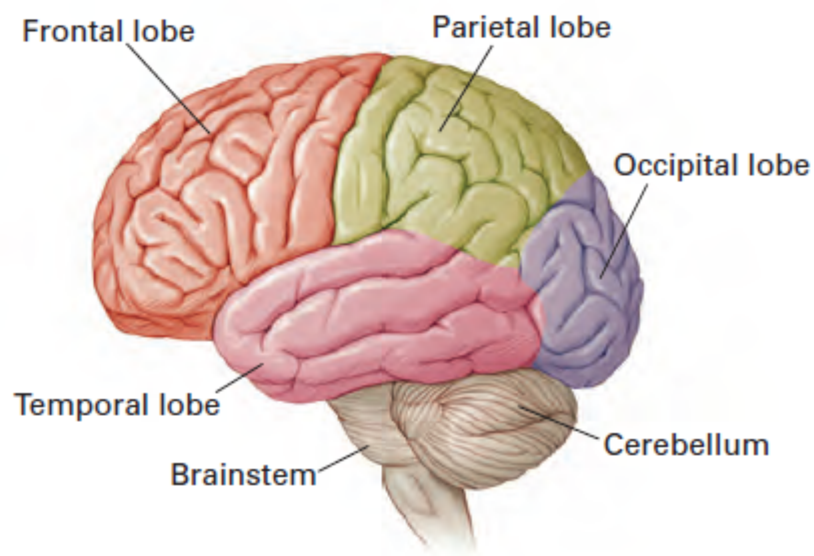
Cerebral cortex *(bark*) – just a very thin layering of cells on the outer surface of the brain

- Thin but heavily folded, squeezing in a lot of surface area
- Plays a role in most voluntary behaviors

Cerebral Cortex



(a)

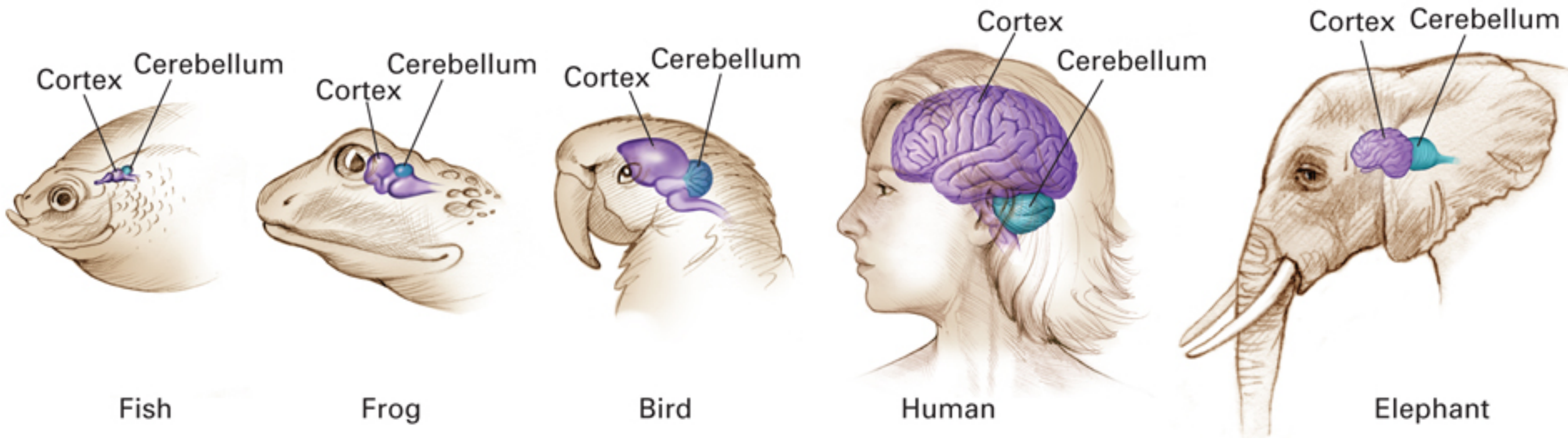


(b)

The four lobes named for the four adjacent bones of the skull:

- **Frontal lobe** – planning and performing complex actions
- **Parietal lobe** – touch, feeling, sense of space
- **Occipital lobe** – vision
- **Temporal lobe** – hearing and remembering

Comparative Neuroanatomy

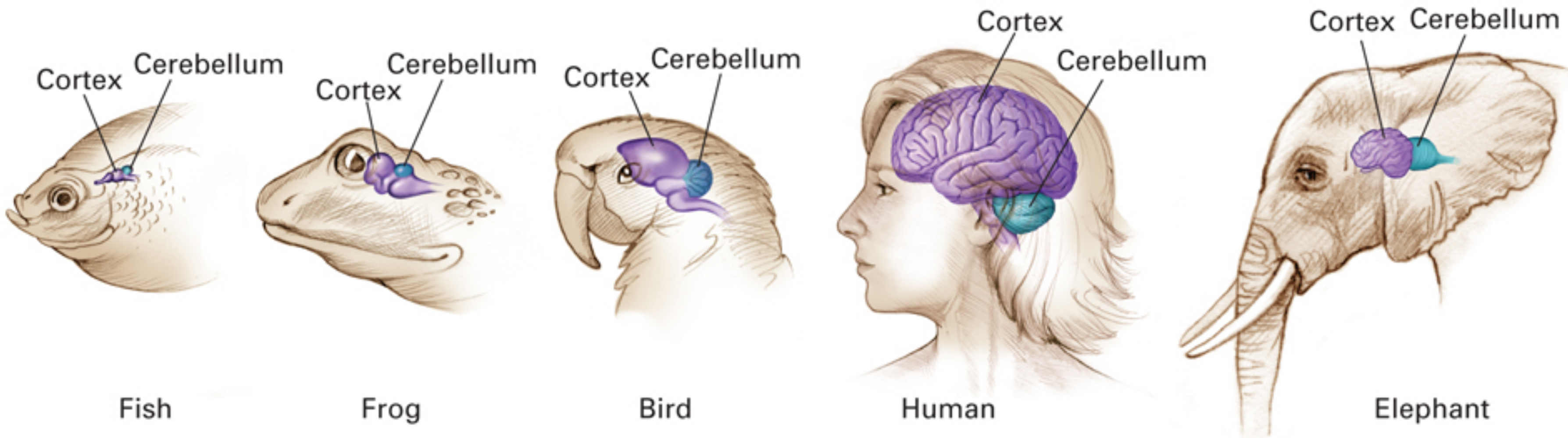


Comparing brains across species gives us some insight into brain function.

First lesson: bigger isn't necessarily better.

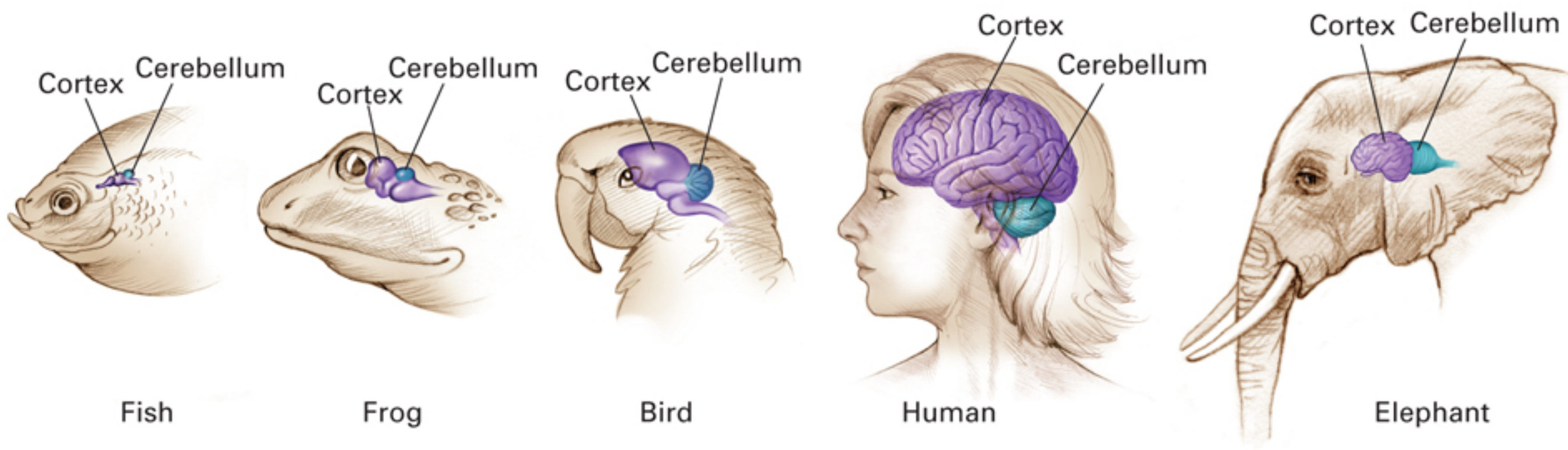
- Elephant brain ~5 kg
- Human brain ~1.4 kg
- Elephants are smart, but would you trade brains with one?

Comparative Neuroanatomy Part 2



- Brains vary not only in overall size, but in relative proportions.
- These differences seem to reflect different specializations for each species' niche.
- For example, birds have bigger proportioned cerebellums than humans, and this may relate to the motor coordination needed for flight.

Comparative Neuroanatomy Part 3



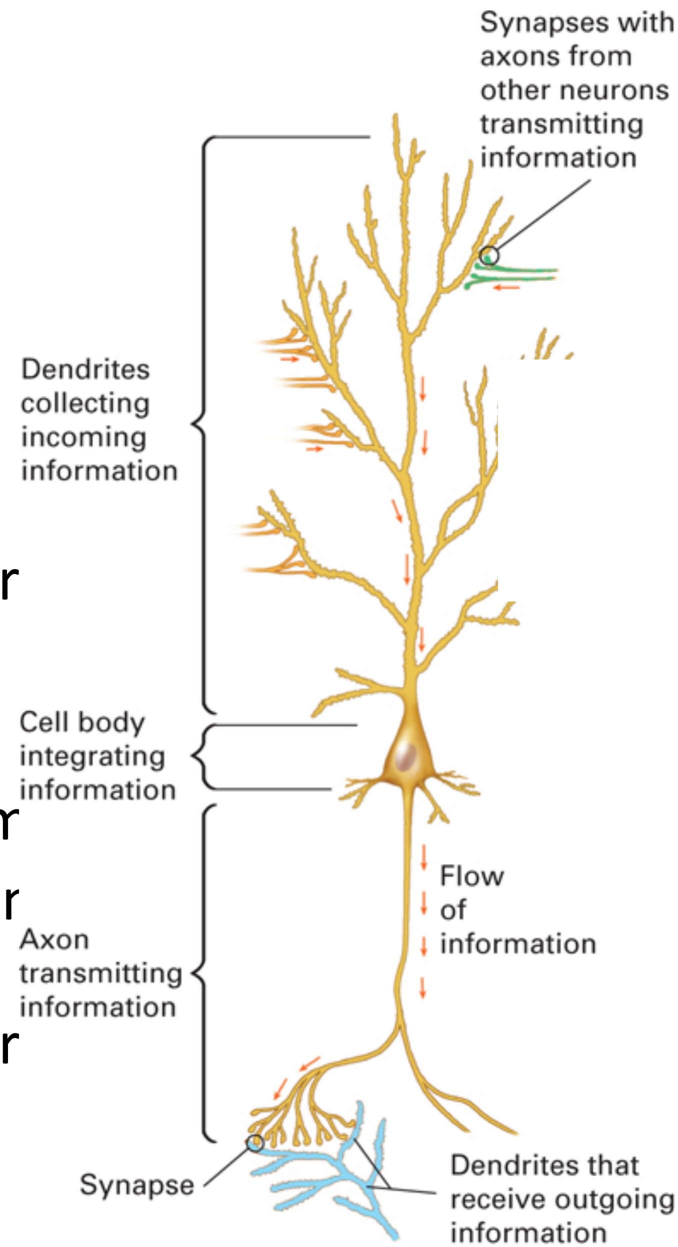
- Relative to other animals, humans have a disproportionately large cerebral cortex.
- Enhanced cortical proportions are shared by other animals we consider clever, such as dolphins and chimps.

Neurons

- Neurons process information:
  - Collect information
  - Process/integrate information
  - Output information
- Neurons (usually) have three basic par
  - Dendrites – collect information
  - Soma (cell body)
  - Axon – integrate and output inform

Neurons have a wide variety of shapes ar processing tasks.

Glia provide support, structure, and nour and outnumber neurons by about 9:1.



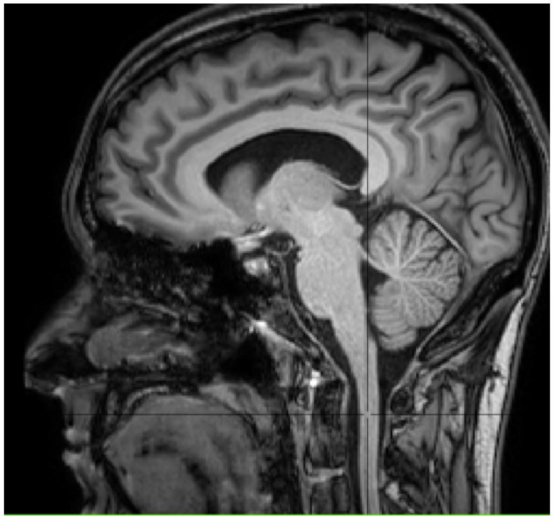
Structural Neuroimaging

- Scientists and physicians have been studying nervous system anatomy since antiquity.
- Until recently, however, studying neuroanatomy could only be done *post mortem.*
- Recently, several non-invasive techniques for structural neuroimaging have been developed: CT, MRI, DTI.
- These techniques allow characterization of **lesions** (areas of brain damage) and tracking of changes due to age, drug abuse, learning, and other factors.

MRI

***MRI = M**agnetic **R**esonance **I**maging*

- Approach:
  - Detection of water density
  - Strong magnetic field aligns water molecules.
  - Radio waves disturb alignment.
  - Relaxation time back to alignment is measured, and this measure depends on density of water in the tissue.
- Results:
  - Extremely detailed 3-D model of the living brain
  - Safe and relatively low cost
  - Has revolutionized medical and scientific research into the brain



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DTI

DTI = D*iffusion* ***T****ensor* ***I****maging*

- Approach:
  - Uses MRI to measure white matter tracts of nerves (brain wiring)
  - Water diffuses well along nerves, but membranes block diffusion through nerves.
  - MRI signal is adjusted to measure diffusion rate of water; nerves are detected as directional preference in diffusion.
- Results:
  - It is possible to reconstruct the connections in the brain, including the strength of these connections.
  - This is a new approach, but there is excitement about understanding how the connections within the brain relate to behavior.

Summary

- The brain and spinal cord make up the vertebrate CNS. The brain controls behavior through connections with the PNS.
- The vertebrate brain is made up of several different regions that contribute to learning and memory.
- Neurons are capable of changing their function and modifying the way they process information.
- Modern structural brain-imaging techniques provide ways to measure variations in the brain structure of living humans without causing harm.
- Techniques for imaging neural structures in nonhumans make it possible to collect detailed information about neural changes that occur during learning.
- Enriched environment studies show that learning experiences can have a profound impact on brain structure and on an individual's learning and memory abilities.

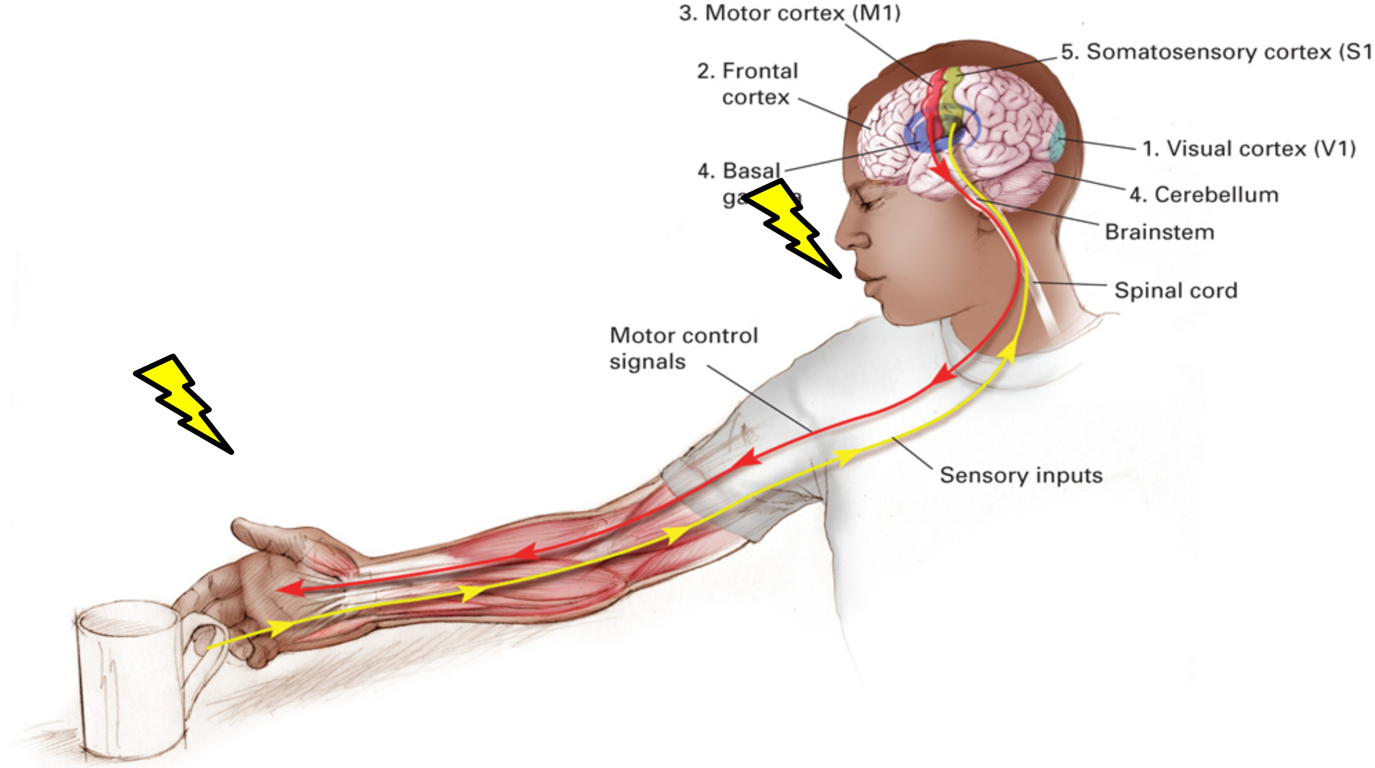
Apply what you know…

Which parts of the brain can you label?

The Neuroscience of Learning and Memory
Part 2

- Structural properties of the nervous system
- Functional properties of learning and memory systems
- Manipulating nervous system activity

What Brains Do



1. Collect sensory information
2. Process information
3. Generate behavior (motor output)

What Brains Do Part 2

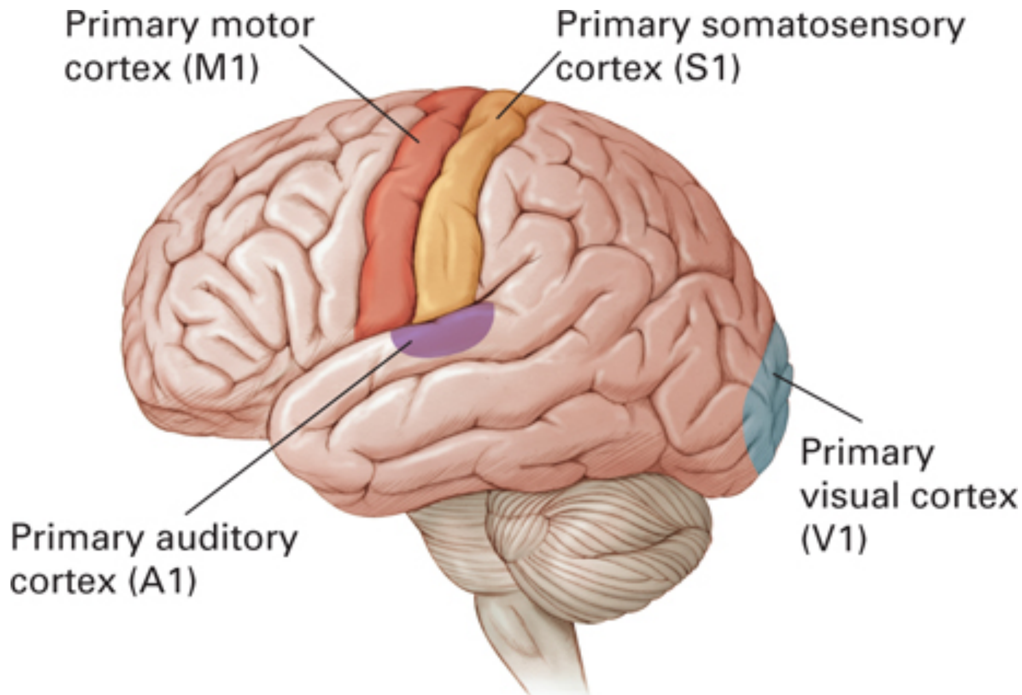
A **reflex** is the simplest expression of the three nervous system functions:

stimulus → little processing → response

Example: finger → little processing → grasp
(palmar reflex in infants)

- Reflexes are hardwired, innate, and involuntary.
- Processing is often handled solely by the spine.

Sensory Pathways

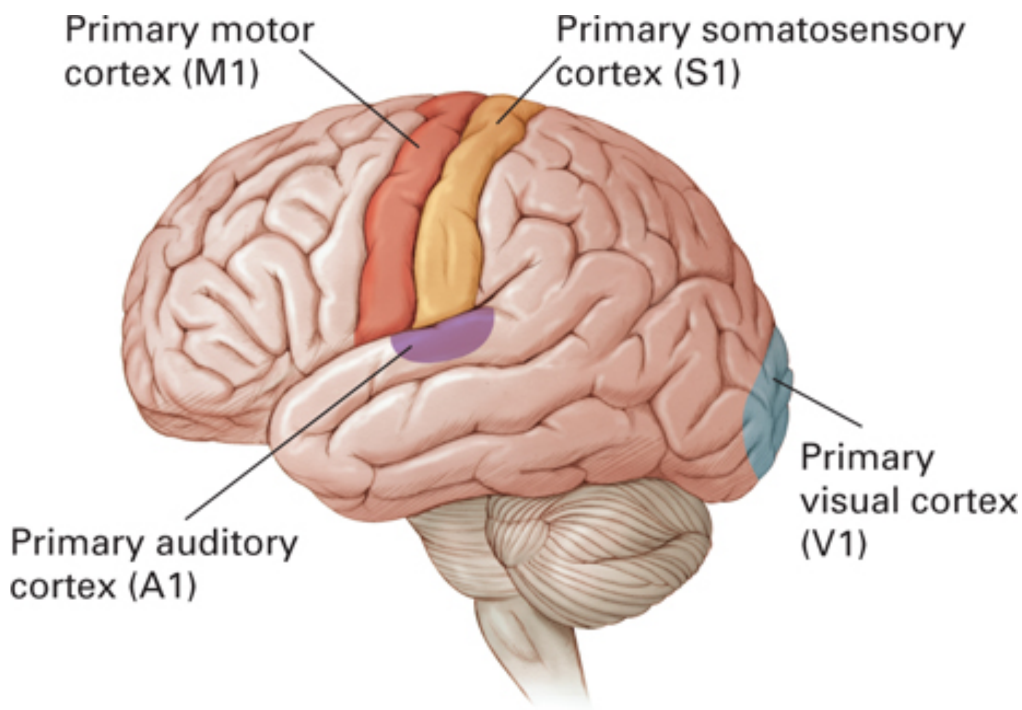


- Common pathway for each sense:

  sensory organs → thalamus → **primary sensory cortex**

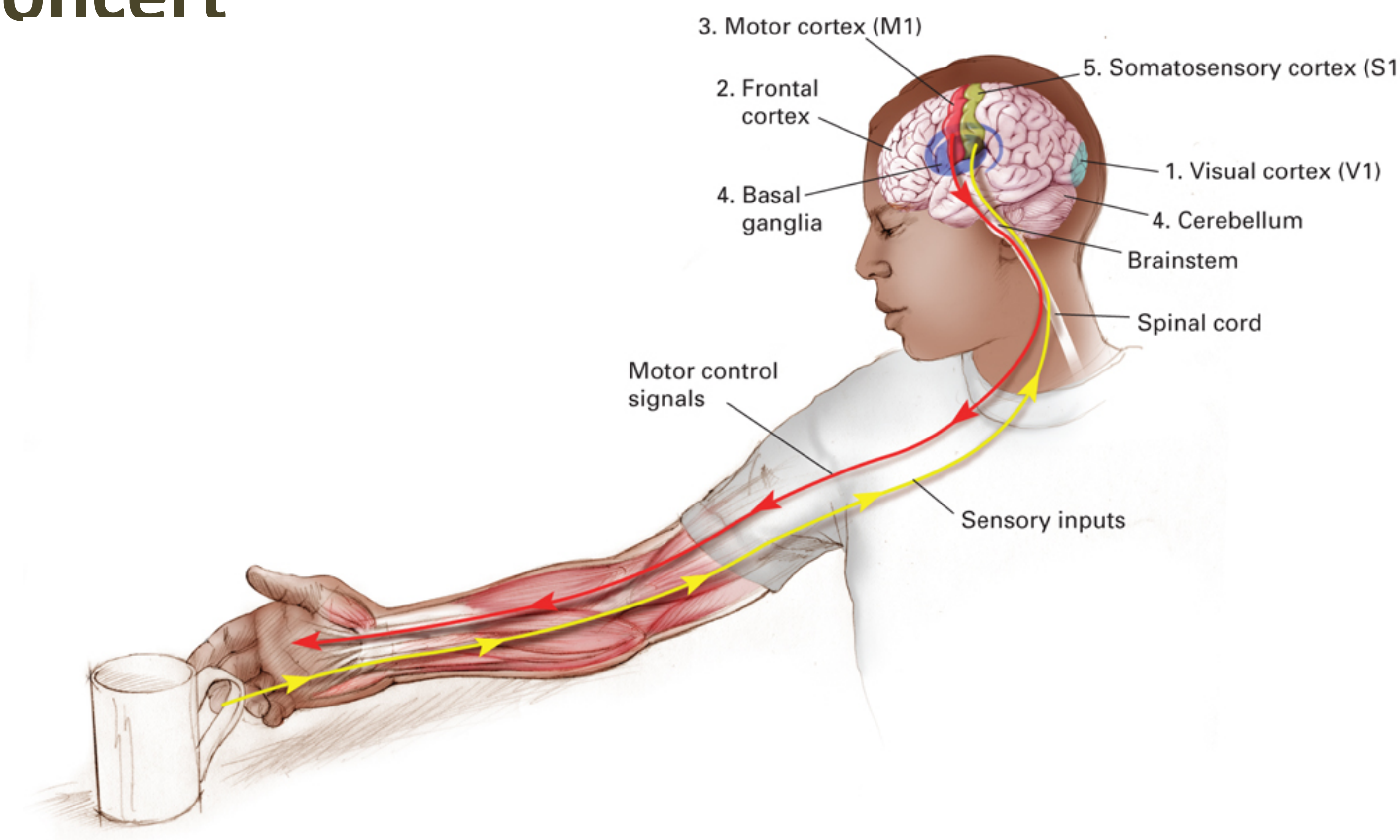
  Example: eyes → thalamus → V1 occipital
- Each primary sensory cortex is specialized for initial processing, then relays on to other cortical areas.

Motor Control



- All voluntary motor output is sent down to the spine via M1, **primary motor cortex**, in the frontal lobe.
- Many inputs to M1 help form behavioral plan:
  - Frontal lobes – planning and logical thinking
  - Cerebellum, basal ganglia – refinements of motor program

Acting in Concert



Outside of simple reflexes, even the most mundane behavior requires the coordination of multiple brain regions and the fine control of many muscles.

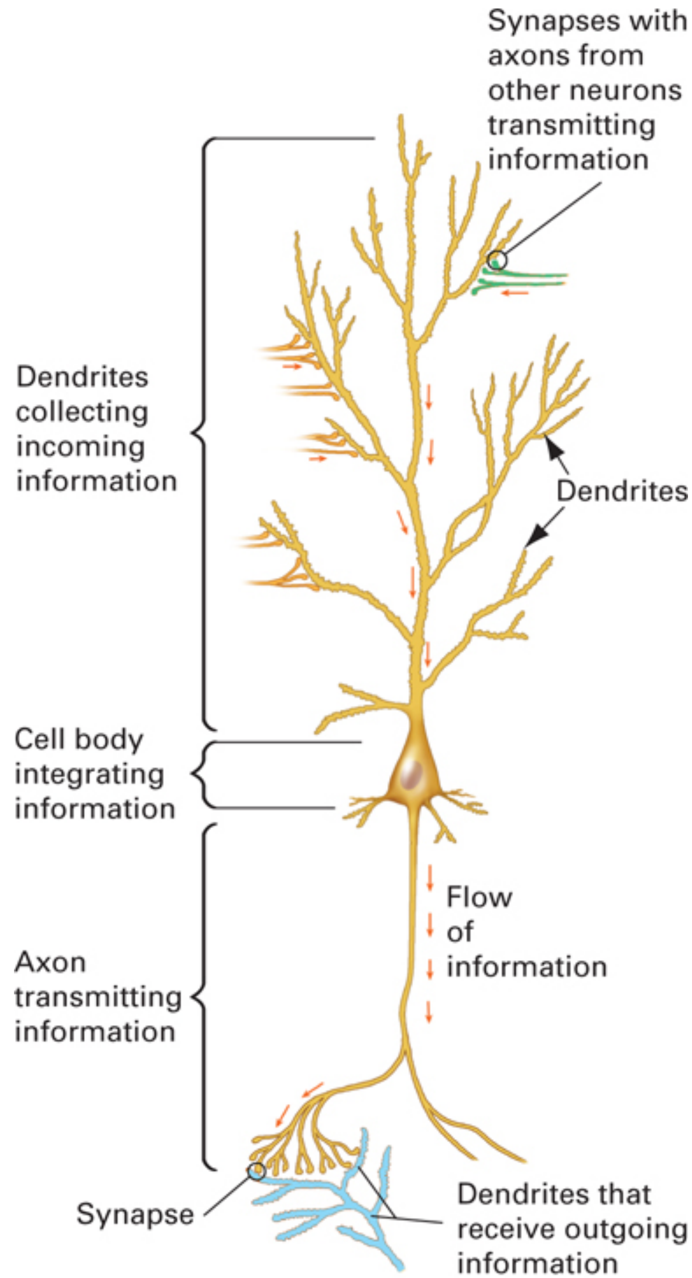
Although some motor programs are innate, humans seem to rely heavily on **learning** to develop coordinated behaviors.

The Neuron: Review

- Neurons process information:
  - Collect information
  - Process/integrate information
  - Output information

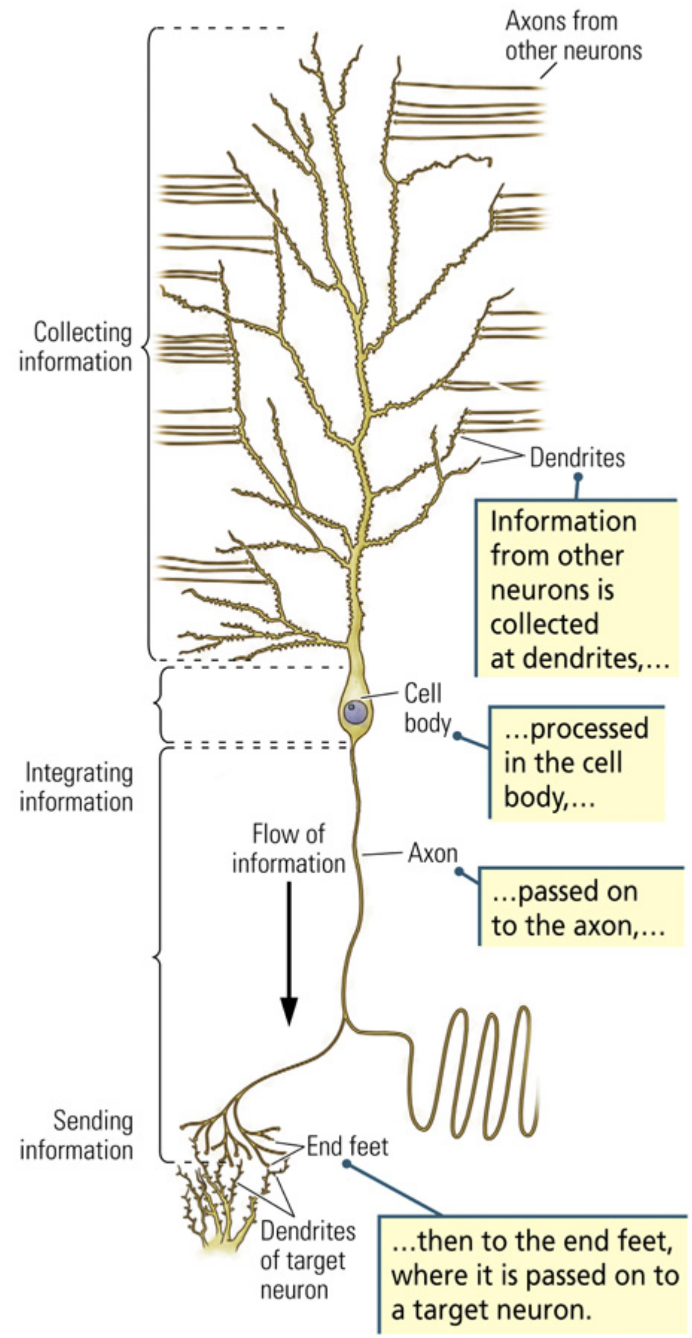
- Neurons have three basic parts:
  - Dendrites – collect information
  - Soma (cell body)
  - Axon – integrate and output information

So how do neurons communicate?



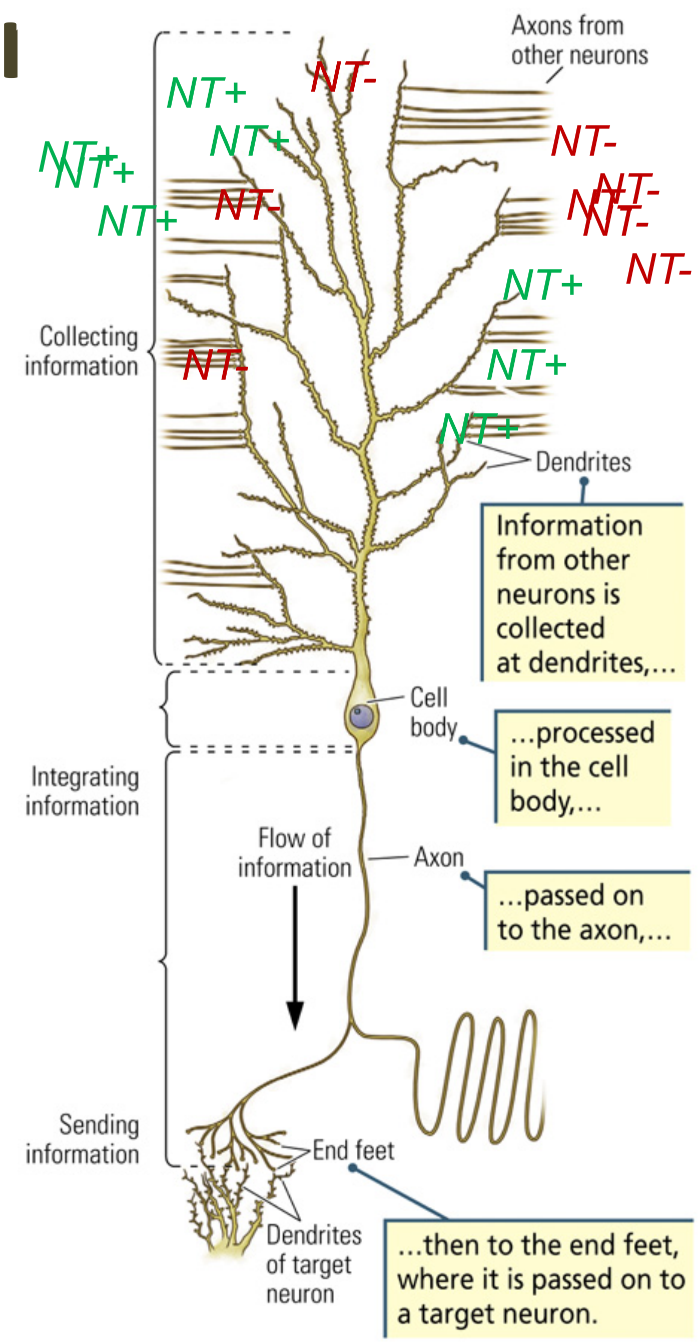
The Neuron

- Neurons speak two languages:
  - Neurotransmitters (chemicals) – with each other
  - Action potentials (electrical) – within a neuron



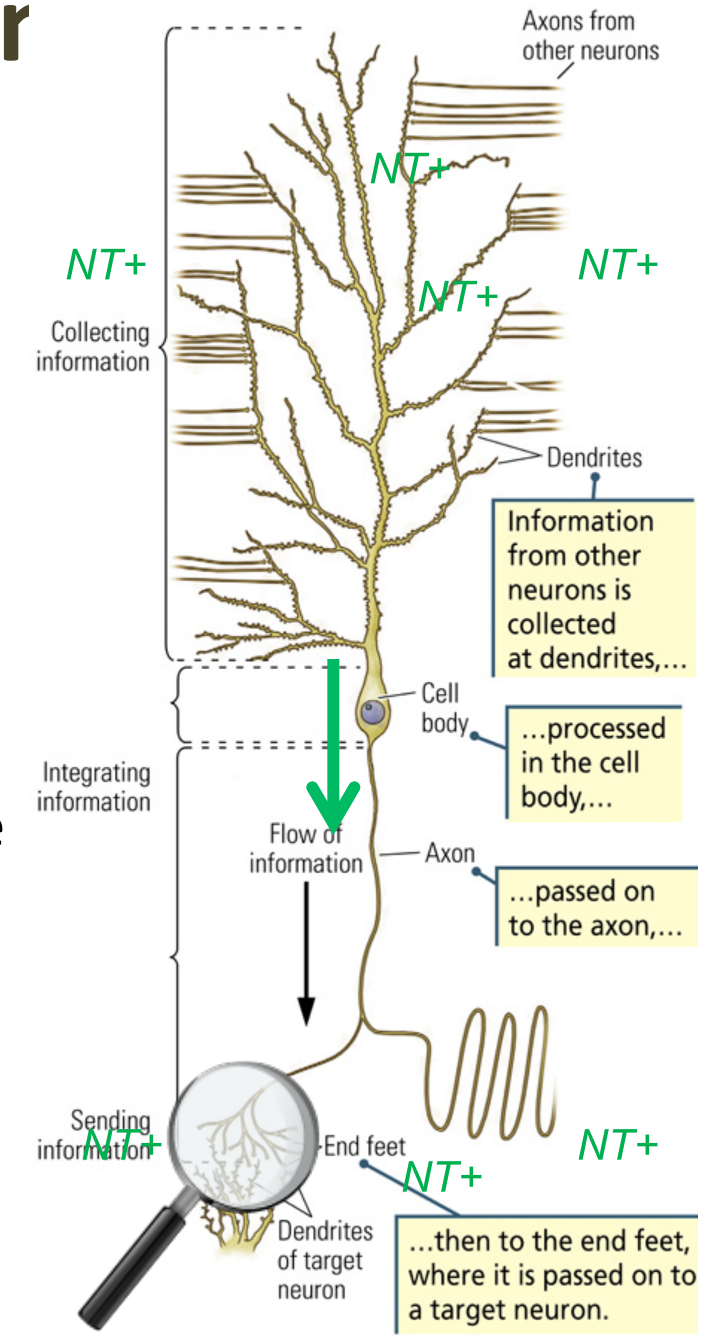
Neural Communicatio

1. Dendrites receive neurotransmitter (NT) signal

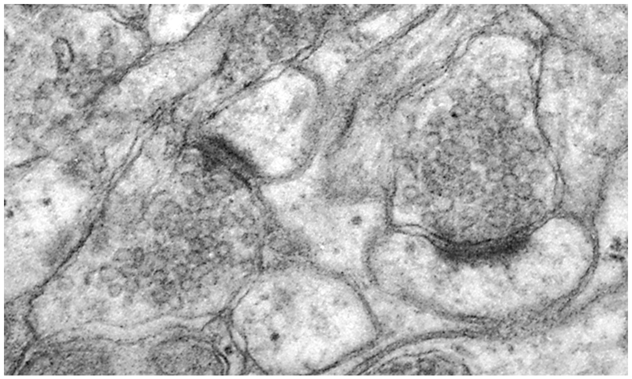


Neuron Communication

1. Dendrites receive neurotransmitter (NT) signal.
2. If excitation > threshold, action potential "fired."
3. Action potential spreads through neuron, causing NT release at all of its synapses.
4. This transmitter affects partner dendrites:
   - Excite – makes an action potential more likely
   - Inhibit – makes an action potential less likely
   - Modulate – alters the neurons in a more lasting way
5. After each action potential:
   - The released transmitter is cleared/ inactivated.
   - There is a very brief **refractory period** during which that neuron can't fire another action potential.



The Synapse



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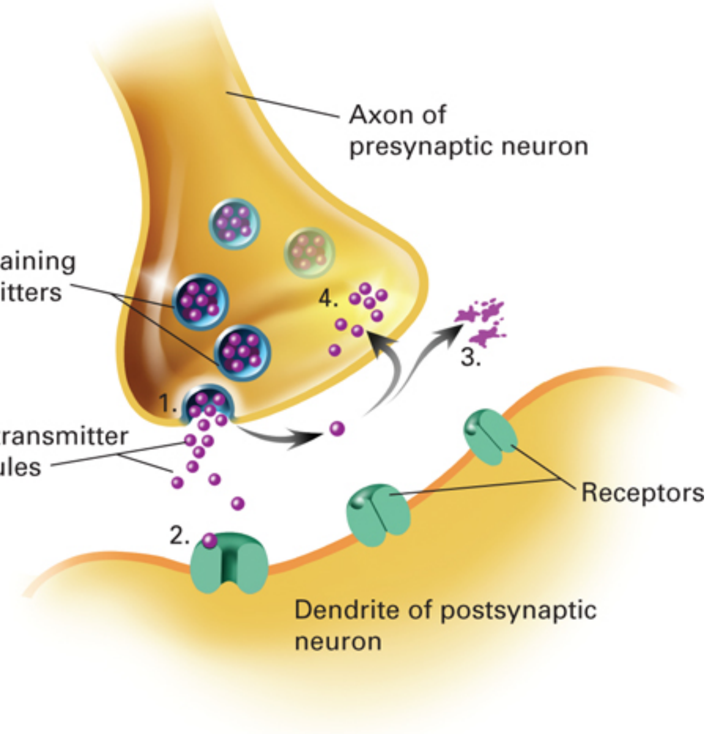
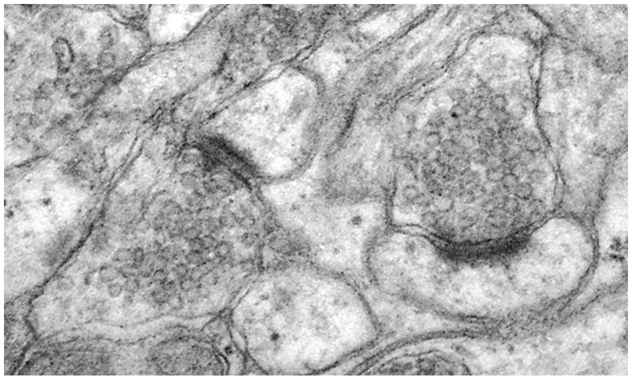


- **Synapse** – The synapse is specialized for chemical communication between axon and dendrite, where the two cells draw very close but don't quite touch (20-nm **synaptic cleft**).
- **Presynaptic side** – The axon has vesicles loaded with neurotransmitters.
- **Postsynaptic side** – The dendrite is studded with receptors to detect the transmitter.

Flexible Communication



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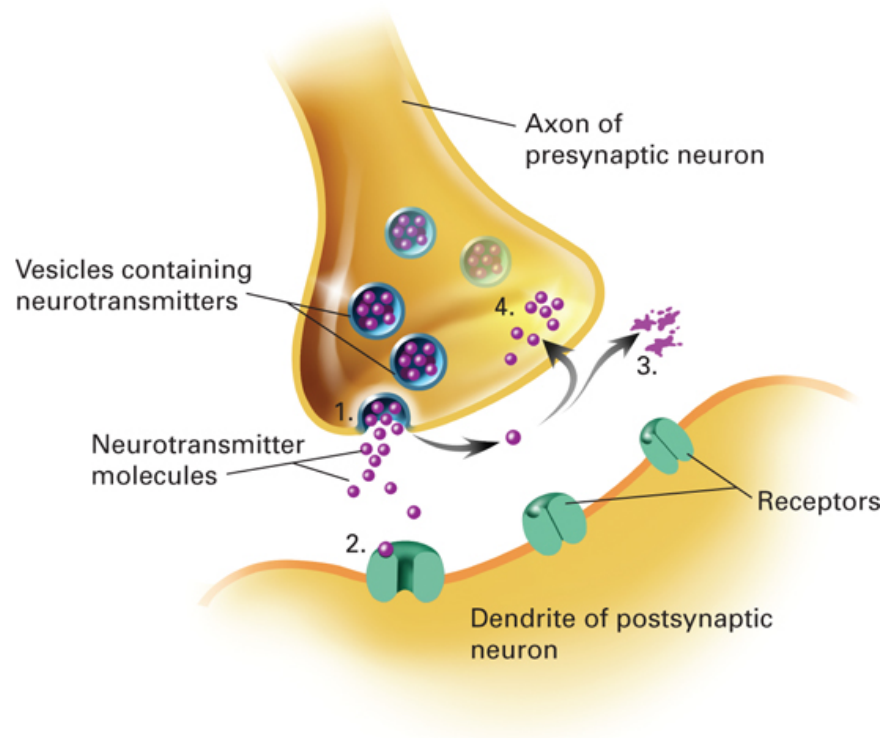


- There are many different neurotransmitters.
- Each transmitter has several different receptors.
- The precise message depends on the specific transmitter and the specific receptor, so many different messages are possible.

Functional Neuroimaging: PET and fMRI

- Functional neuroimaging techniques track localized brain activity.
- However, the measures are **indirect**:
  - Heavy brain use recruits additional blood flow (**hemodynamic response**) to provide the additional nutrients needed to support activity.
  - Functional imaging tracks markers related to these blood-flow changes.
  - Because blood-flow changes more slowly and more subtly than activity, these techniques are less sensitive in time and space than electrophysiology.
- Two major techniques are in use:
  - PET (positron emission tomography) – injects a radioactive tracer to the blood
  - fMRI (functional MRI) – same as anatomical MRI, but signal detected relates to blood oxygenation

Positron Emission Tomography (PET)

- Radioactive tracer is injected into the bloodstream.
- As brain areas use more blood, more radioactive tracer enters the area.
- This is detected by a ring of scanners and reassembled into a 3-D portrait of the brain.
- Thus, PET measures regional cerebral blood flow (rCBF) but indicates activity.

Positron Emission Tomography (PET) Part 2

Problems

Radioactivity! Limited trials/ person

Spatial resolution

- 2–3 mm per subject
- Averaged across subjects: 10 mm
- Relatively poor

Blood flow takes ~30 s to change.

- One action potential takes 1 ms
- Thus, relatively poor **temporal resolution**

Functional Magnetic Resonance Imaging (fMRI)

Advantages:	Disadvantages
• High spatial resolution: 1 mm or more with stronger magnet • Temporal resolution: ~1–4 s before blood level change is sufficient to measure • No radiation • Simple and relatively cheap • No risk, so longer experiments okay	• Only tracking blood flow, which is slow and not that precise • Ongoing brain activity • Brain differences

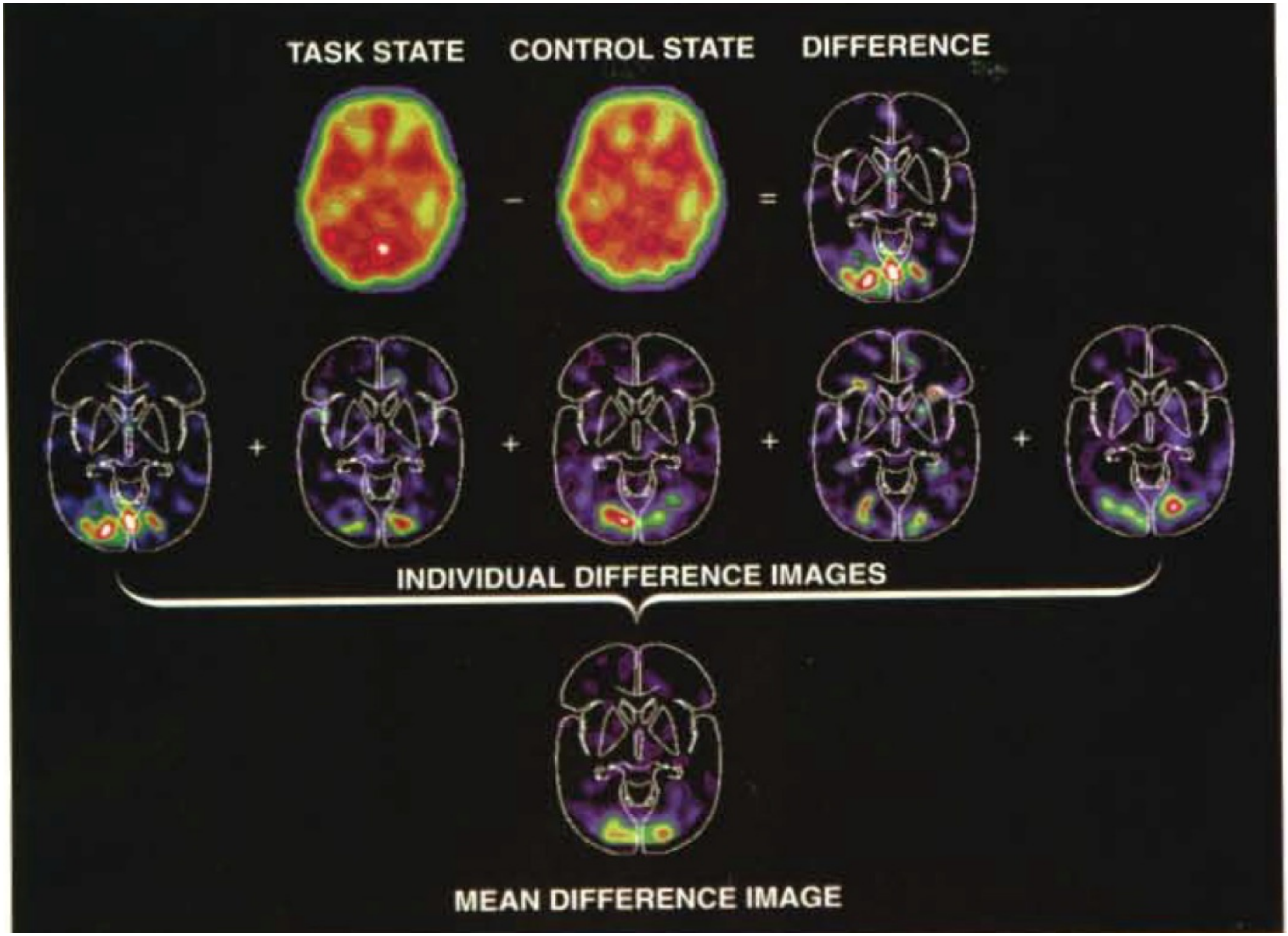
EEG - Electroencephalography

EEG measures electrical activity non-invasively, through electrodes placed on the scalp.

Pros - Fast, non-invasive measure of overall brain activity (sleep, wake, coma)

Cons – Weak, noisy signal reflecting large portions of the brain all at once; so far, can only read general brain states

Brain Images



M.E. Raichle, Mallinckrodt of Radiology, Washington University School of Medicine

Functional Neuroimaging: PET and fMRI Part 2

- Both PET and fMRI suffer from a major drawback: ongoing brain activity.
  - Contrary to popular belief, you are using your whole brain all the time.
  - A typical scan shows basically the whole brain heavily using blood.
- The problem is overcome with the subtraction technique: measure changes in blood flow as the behavioral task changes.

  Example: listen words – listen noise = activity specific for hearing words

Summary Part 1

- Reflexes are natural, automatic responses to stimuli. Early neuroscientists believed that all complex learning involved combining simple spinal reflexes.
- In the brain, sensory signals are initially processed in cortical regions specialized for processing such signals and lead to activity in other cortical regions that are specialized for coordinating movements.
- The neural transmission that enables stimuli to generate responses takes place across synapses: the presynaptic neuron releases neurotransmitters into the synapse; these chemicals cross the synapse to activate receptors on the postsynaptic neuron.

Summary Part 2

- Functional neuroimaging methods allow researchers to track brain activity during the performance of memory tasks by measuring changes in glucose utilization and blood oxygenation in different brain regions.
- Electroencephalographic recordings make it possible to track the activity of large populations of neurons over time.
- Single-cell recordings allow researchers to directly monitor and record the electrical activity of single neurons and changes in their firing patterns that occur during learning or the recall of memories.

Apply what you know

Botulinum toxin (commonly known as Botox) prevents action potentials from being able to release neurotransmitters into the synaptic cleft.

How would botulinum toxin affect communication between neurons?

If you wanted to disrupt visual processing, what area of the brain could you target with botulinum toxin?

As a cosmetic, botulinum toxin is injected in small doses into facial wrinkles. Which function of the nervous system is being targeted?

The Neuroscience of Learning and Memory Part 3

- Structural properties of the nervous system
- Functional properties of learning and memory systems
- Manipulating nervous system activity

Brain Parts and Their Function

- How do we know what a specific region of the brain does?
- One clue comes from **neuropsychology** studies of human patients with specific brain lesions (brain damage):
  - Determine area of brain region (e.g., with MRI).
  - Do tests to determine what behavioral abilities are impaired.
  - Tentatively conclude that the damaged brain region is responsible for the impaired behaviors.

Brain Parts and Their Function Part 2

- Animal models for neuropsychology:
  - Experimentally create a brain lesion, even mimicking damage in human patients.
  - Do tests to determine what behavioral abilities are impaired.
  - Tentatively conclude that the damaged brain region is responsible for the impaired behaviors.

  Example: Rats given damage to the hippocampi seem unable to learn new facts.

Brain Parts and Their Function Part 3

- Although lesion methods in human and animal models are suggestive, they must be interpreted with caution.

  Example: Lashley's search for the engram
  - Trained rats to run a maze
  - Lesioned section of cortex
  - Re-tested for memory of maze
  - Found that only very large lesions disrupted function
- But …
  - Only lesioned cortex! Failed to test other brain areas.
  - Also, test wasn't sensitive: rats could learn to run it by sight, smell, and even touch, so small memory problems weren't being detected.

Can you think of other design/ interpretation problems with these methods?

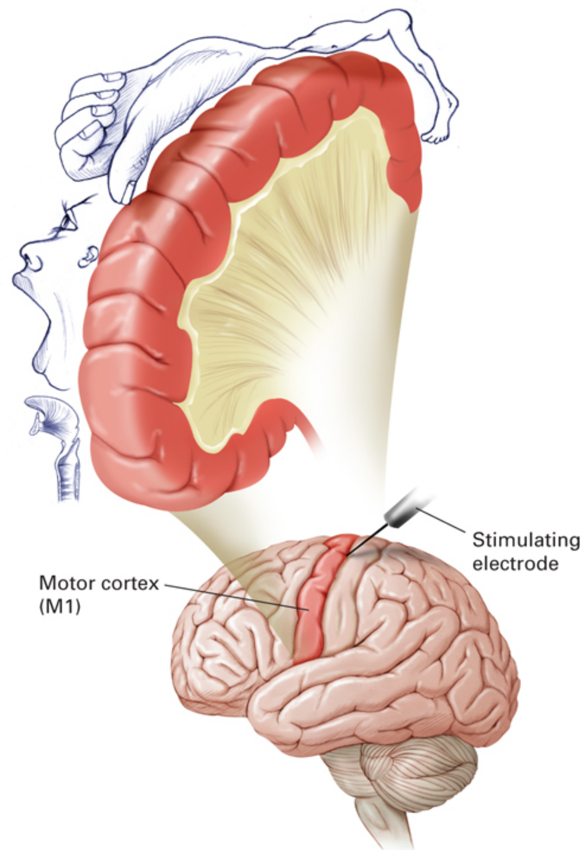
Neurophysiology

- Direct implantation of wires into the brain allows both recording and stimulation of single neurons.
- Although invasive, recordings can provide a direct readout of neural communication, making it possible for scientists to “decode” the information being processed in the brain.
- When stimulating neurons, scientists can observe the effects of activating discrete brain areas and even single neurons.

Neurophysiology Part 2

Stimulation of M1 reveals a distorted "body map" of muscle control.

Natural History Museum, London, UK / The Image Works



Got anything less invasive?

Chemical Control of Brain States

- Drug consumption is the most ancient technique for altering the brain.
  - Mimic neurotransmitters (agonist)
  - Block receptors (antagonist)
  - Change synthesis
  - Change recycling
  - Many other possible effects on neural communication

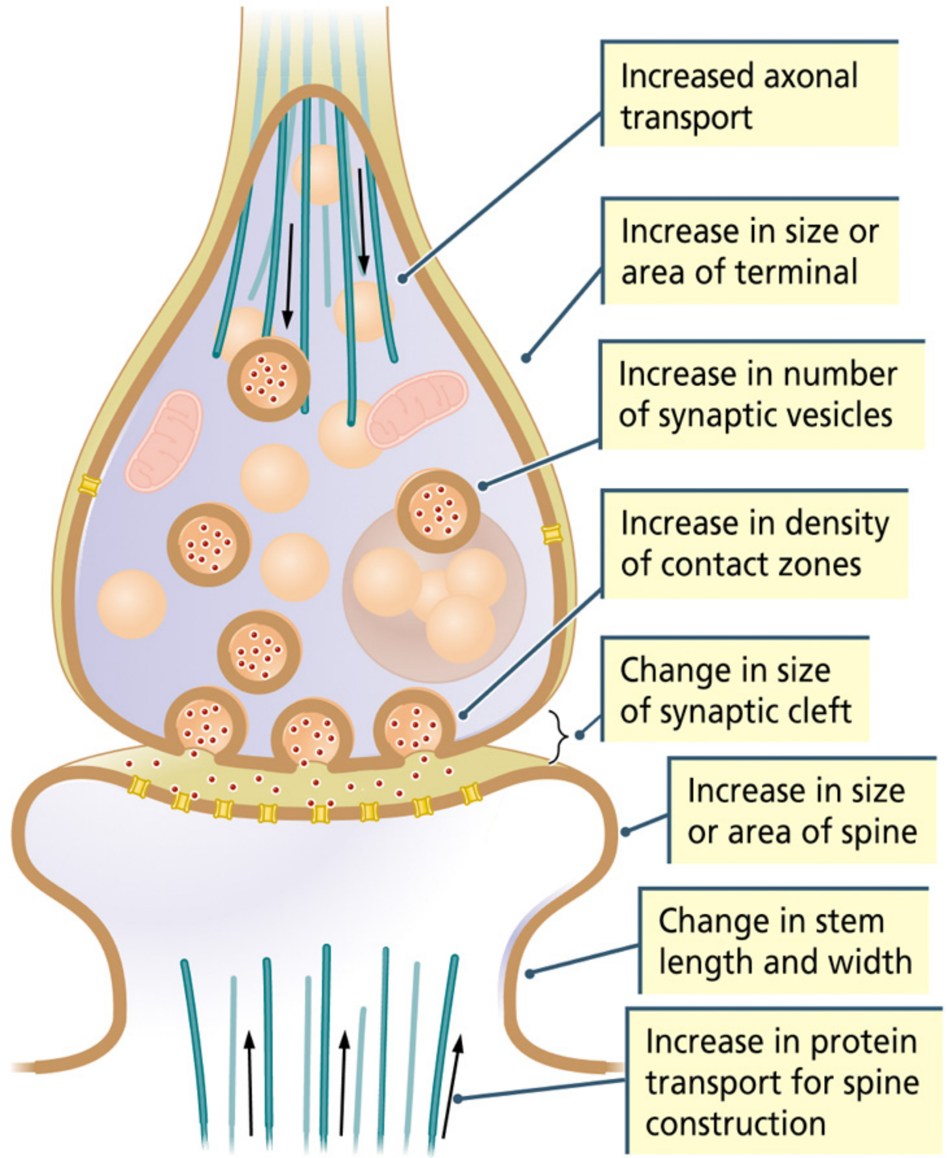
Pros:
- Interfaces with the chemical language of the brain
- Different chemicals for producing different effects

Cons:
- Not selective to brain region or even to the brain
- Brain can adjust to chemical changes

What about tapping into the electrical language of the brain?

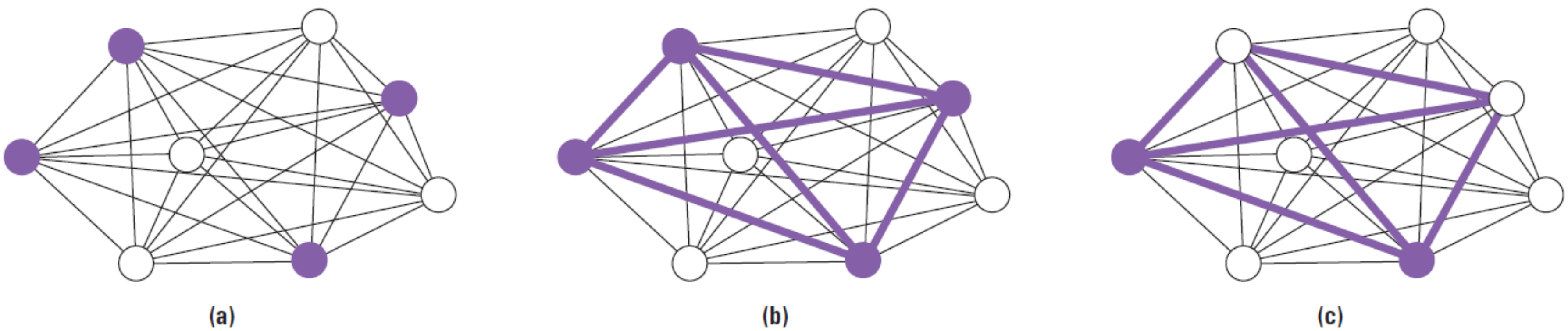
Synaptic Plasticity

- Any physical change in neurons can affect how they communicate and how brain systems interact.
- However, synapses can change as a result of experience, known as **synaptic plasticity.**
- *"Neurons that fire together, wire together"*



Hebbian Learning

Learning that involves strengthening connections between neurons that work together is called **Hebbian learning**.



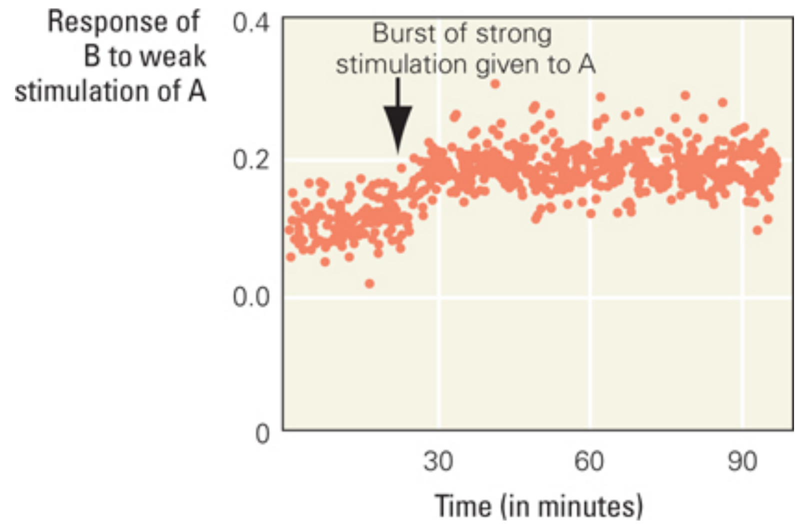
- Circles correspond to cortical neurons; lines are connections between them.
- Stimulus input activates a subset of neurons.
- Connections by coactive neurons are strengthened.
- After connections between coactive neurons are established, a stimulus may activate some of the neurons.

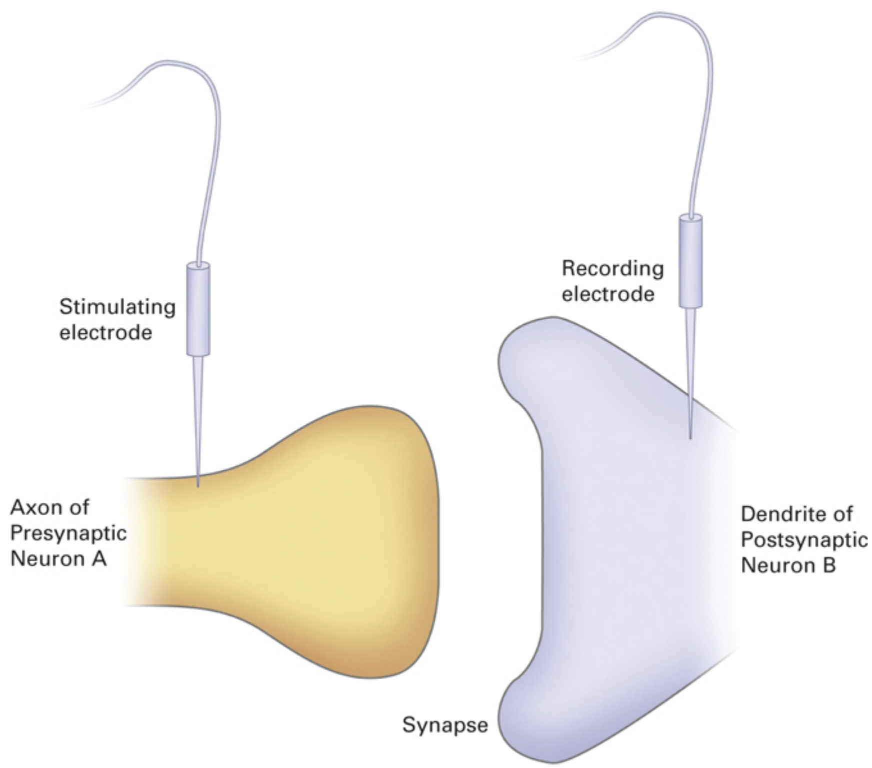
Synaptic Plasticity Part 2

***LTP – long-term potentiation**:* when two neurons fire at same time repeatedly, synapses between them get stronger (fire together, wire together).

LTD – long-term depression: when two neurons fire out of sync, synapses between them get weaker (out of sync, lose link).

Synaptic Plasticity Part 3





Strong firing in A (at arrow) causes joint activity in A and B. This causes LTP in the connection between these neurons.

Synaptic Plasticity Part 4

- In the long term, both LTP and LTD involve not only local synaptic changes, but physical restructuring of neurons:
  - LTP – sprouting of new synaptic contacts between co-activated neurons
  - LTD – retraction/dismantling of synaptic contacts between non-cooperating neurons

Summary Brain Parts

- Accidental brain lesions in humans (and intentional in animals) have revealed how brain regions function and contribute to learning and memory.
- Researchers can use implanted electrodes to stimulate neurons and then observe sensations or responses.
- Drugs are chemicals that alter the biochemical functioning of the body and affect neural activity by interfering with synaptic transmission.
- The ability of synapses to change with experience is called synaptic plasticity.
- LTP occurs when synaptic transmission becomes more effective as a result of strong electrical stimulation of neurons.
- LTD occurs when synaptic transmission becomes less effective after neurons do not fire together.